

# Aging & Rehabilitation

## An Interdisciplinary Research Seminar Series



# Sponsors

## Department of Veteran Affairs

- Rehabilitation Outcomes Research Center (RORC)
- Brain Rehabilitation Outcomes Research Center (BRRC)
- Geriatric Research, Education, and Clinical Center (GRECC)

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- Department of Aging and Geriatric Research

## UF College of Public Health and Health Professions

- Brooks Center for Rehabilitation Studies

## UF College of Liberal Arts and Sciences

- Center for Gerontological Studies

## UF McKnight Brain Institute

## UF College of Nursing

# Schedule

- January 9<sup>th</sup>, 2006 – May 22<sup>nd</sup>, 2006
- Mondays, 12:00 – 1:00
- Location: UF HPNP Building, Room G101
- Cyber Seminar:
  - VA RORC Conference Room, Commerce Building Downtown
  - VA BRRC Nursing Home Care Unit Conference Room (first floor)
  - UF Brooks Center Conference Room, Jacksonville (904) 306-8977

# Themes

- Basic Science
- Clinical Science
- Outcomes / Health Policy
- Behavioral and Social Research
- Cutting Edge / New Research

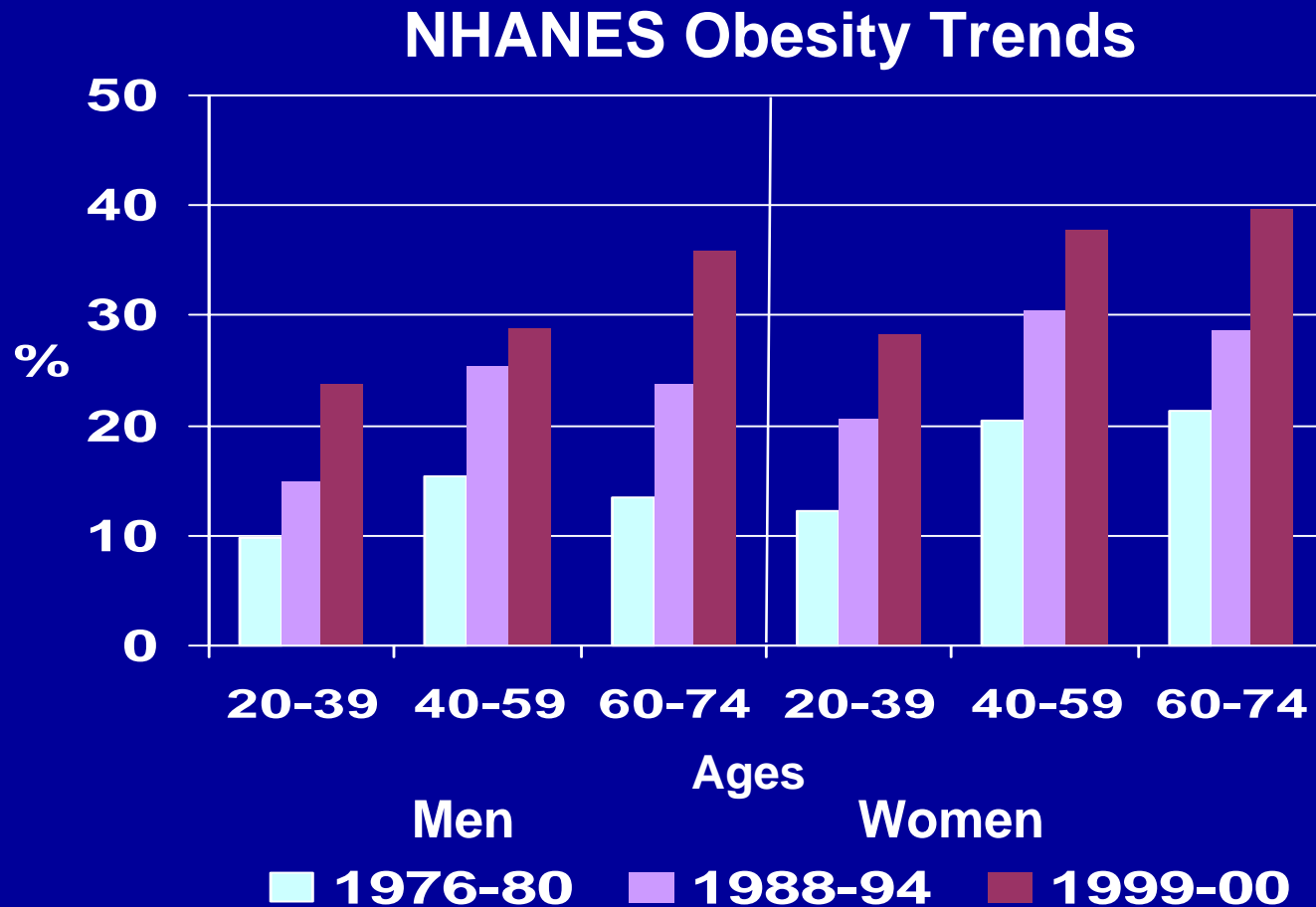
# Sarcopenia in the Obesity Era

Stephen B. Kritchevsky, PhD

Sticht Center on Aging

Wake Forest University School of Medicine

# The prevalence of obesity is growing across all age groups



(Flegal et al, JAMA, 2002)

# Sarcopenia (Abbreviated Version)

- Muscle mass is lost progressively after young to mid-adulthood.
- Muscle mass correlates with strength.
- Low strength is a hallmark of disability.
- Many disabling conditions are associated accelerated with the loss of lean mass.
- The Sarcopenia concept was articulated before the importance of fat as an endocrine organ had been fully realized.

# Health ABC Design

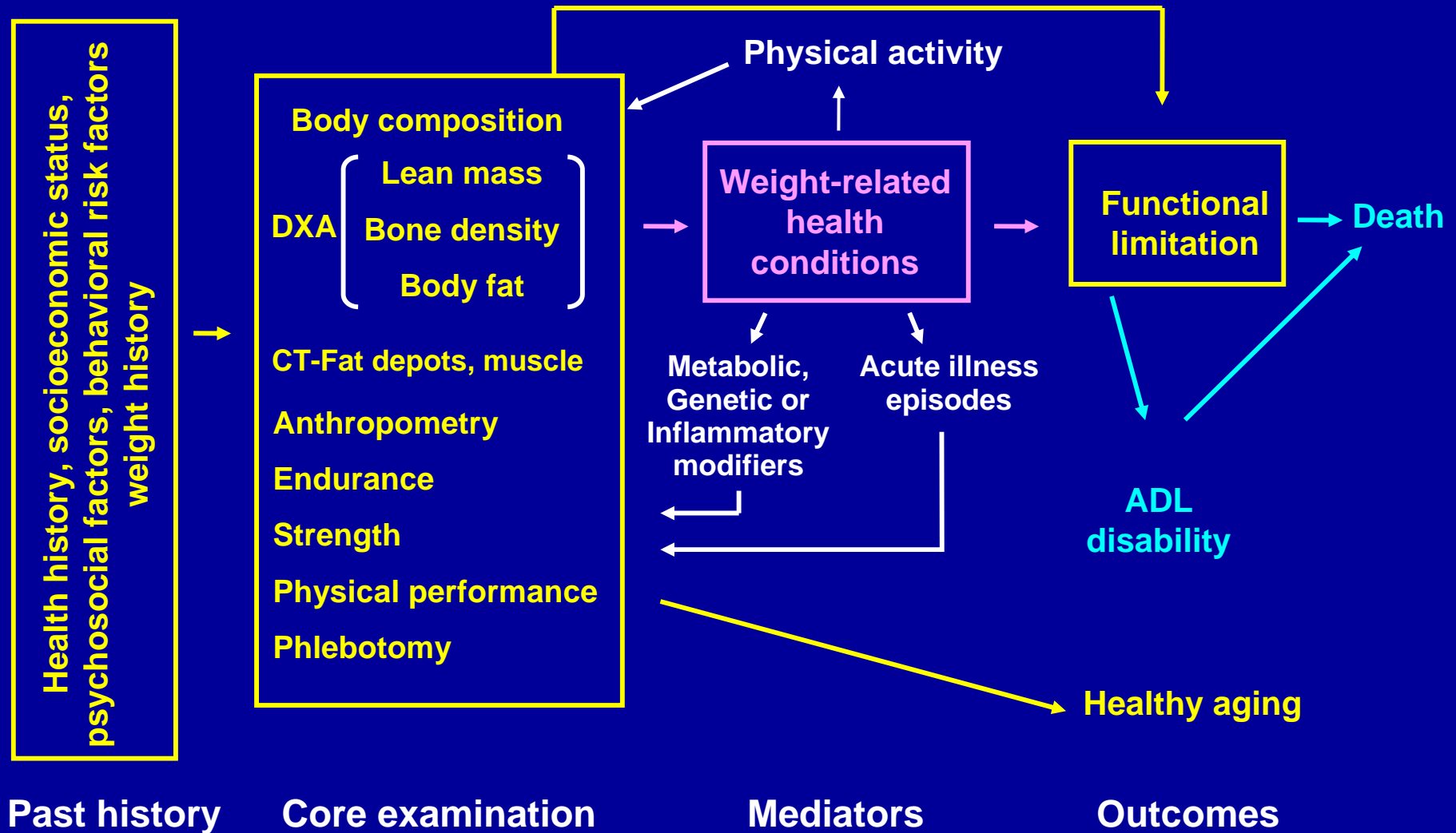
- Longitudinal Cohort Study

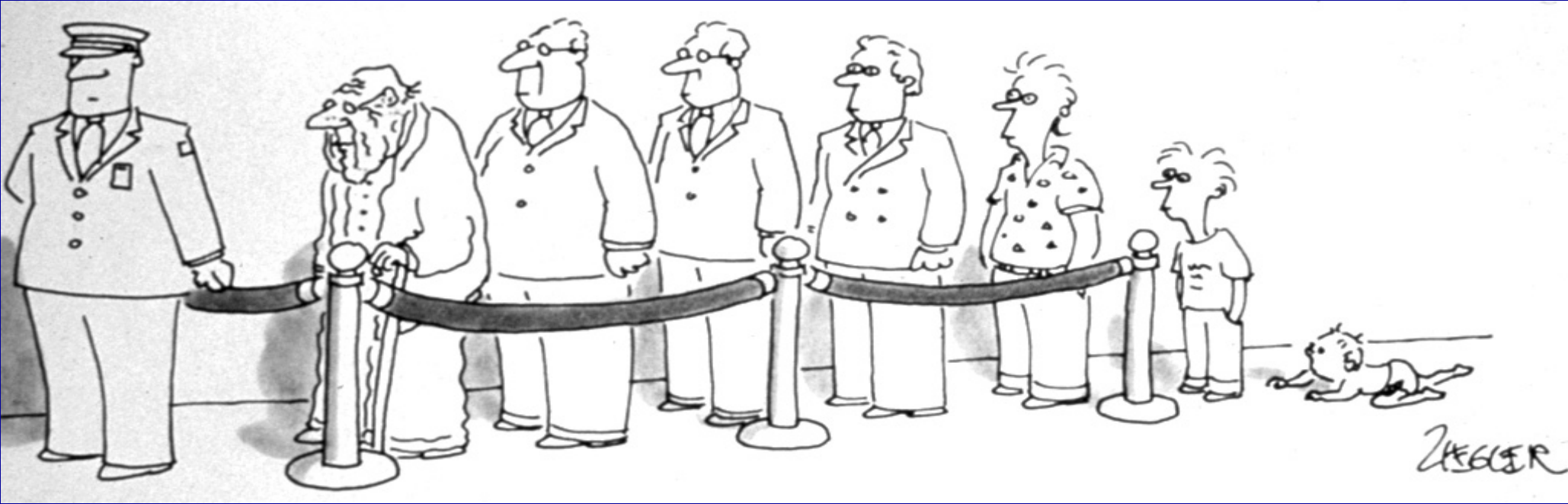
- N=3,075
- 70-79 year olds
- Memphis, TN & Pittsburgh, PA
- No difficulty in walking  $\frac{1}{4}$  mile or climbing 10 steps
- 50% Women, 42% African-American
- Beginning its 9th year of follow-up

# Health ABC Design (Continued)

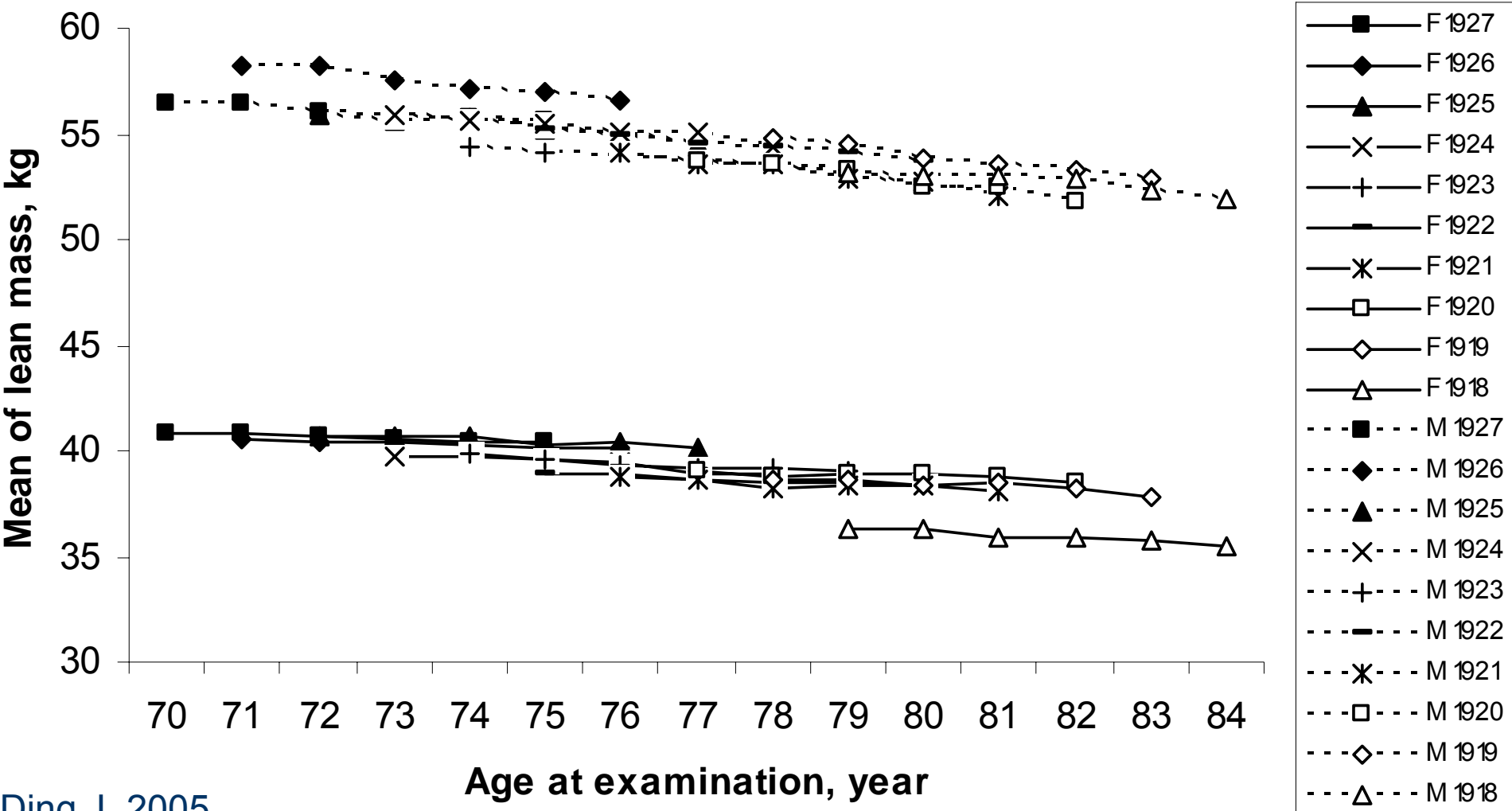
- **Primary Outcome (Lower Extremity Functional Limitation)**
  - Any difficulty walking  $\frac{1}{4}$  mile or going up 10 steps over a 6-month period
- **Secondary Outcomes**
  - Disability, Mortality, Weight Related Health Conditions
- **Visit Schedule**
  - Annual Clinic Visits
  - Phone Contact

# Health, Aging and Body Composition Study

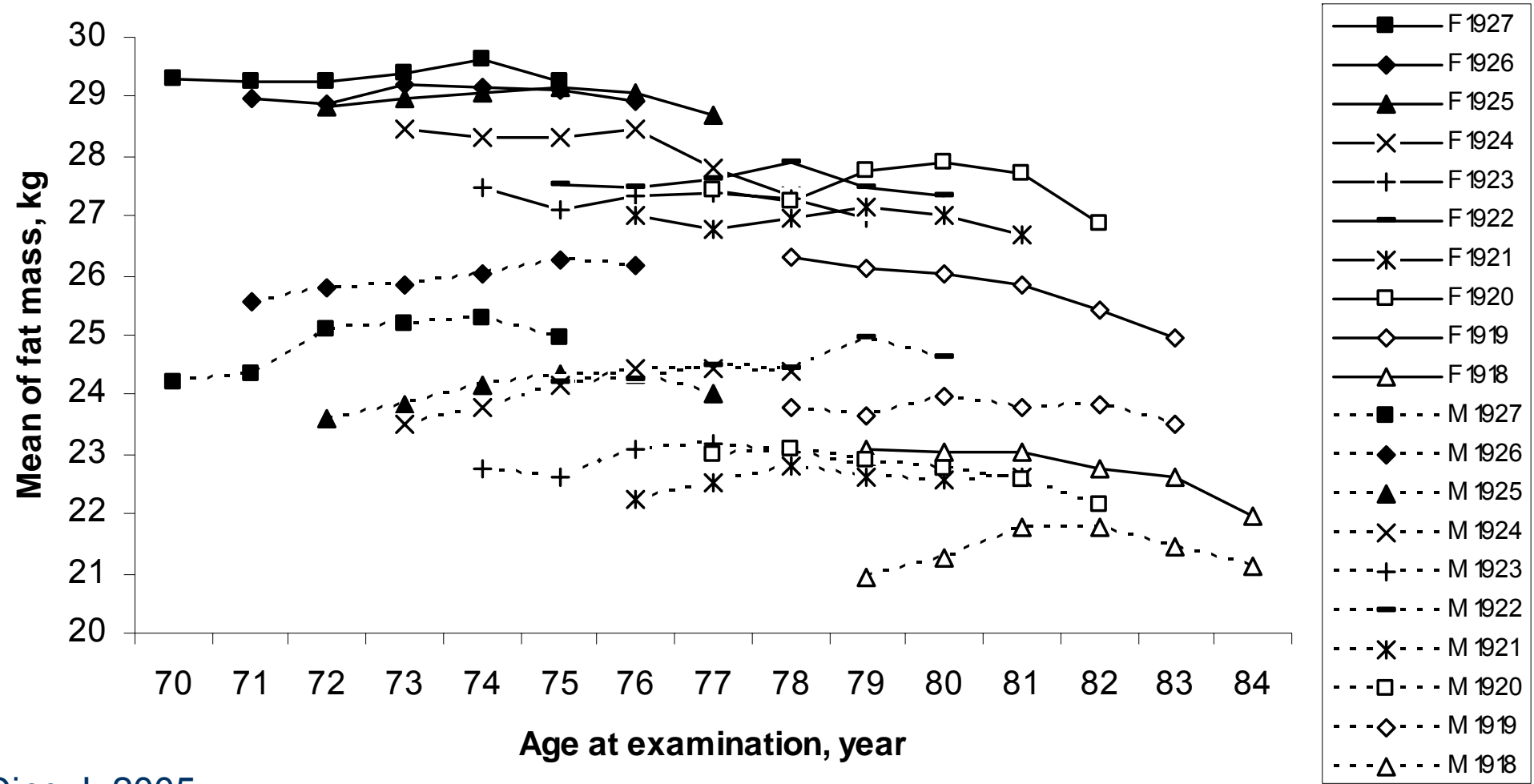




**Means of lean mass by age at examination (70-84 years) and birth cohorts (year 1918-1927) for 855 men (M) and 931 women (F) who participated in all 6 DXA examinations during the 5-year follow-up in the Health ABC Study**



**Means of fat mass by age at examination (70-84 years) and birth cohorts (year 1918-1927) for 855 men (M) and 931 women (F) who participated in all 6 DXA examinations during the 5-year follow-up in the Health ABC Study**



## Cohort effect and age-related changes in percent body fat, fat mass, and lean mass in Health ABC participants with complete body composition assessments.

	Birth cohort		Age at examination		Age at examination <sup>2</sup>	
	$\beta$ (SE) †	p	$\beta$ (SE) †	p	$\beta$ (SE) †	p
<b>Men (N = 855)</b>						
<b>Percent body fat</b>	<b>0.32 (0.06)</b>	<b>&lt;0.0001</b>	<b>0.40 (0.05)</b>	<b>&lt;0.0001</b>	<b>-0.01 (0.003)</b>	<b>&lt;0.0001</b>
<b>Fat mass, kg</b>	<b>0.45 (0.09)</b>	<b>&lt;0.0001</b>	<b>0.40 (0.06)</b>	<b>&lt;0.0001</b>	<b>-0.02 (0.003)</b>	<b>&lt;0.0001</b>
<b>Lean mass, kg</b>	<b>0.17 (0.09)</b>	<b>0.05</b>	<b>-0.18 (0.04)</b>	<b>&lt;0.0001</b>	<b>-0.008 (0.002)</b>	<b>0.005</b>
<b>Women (N = 931)</b>						
<b>Percent body fat</b>	<b>0.16 (0.07)</b>	<b>0.02</b>	<b>0.19 (0.05)</b>	<b>&lt;0.0001</b>	<b>-0.01 (0.003)</b>	<b>&lt;0.0001</b>
<b>Fat mass, kg</b>	<b>0.34 (0.10)</b>	<b>0.001</b>	<b>0.20 (0.06)</b>	<b>0.0006</b>	<b>-0.02 (0.004)</b>	<b>&lt;0.0001</b>
<b>Lean mass, kg</b>	<b>0.18 (0.07)</b>	<b>0.006</b>	<b>-0.09 (0.03)</b>	<b>0.005</b>	<b>-0.002 (0.002)</b>	<b>0.25</b>

Mixed model including birth cohort, age at examination, age at examination<sup>2</sup>, race, and clinic site.

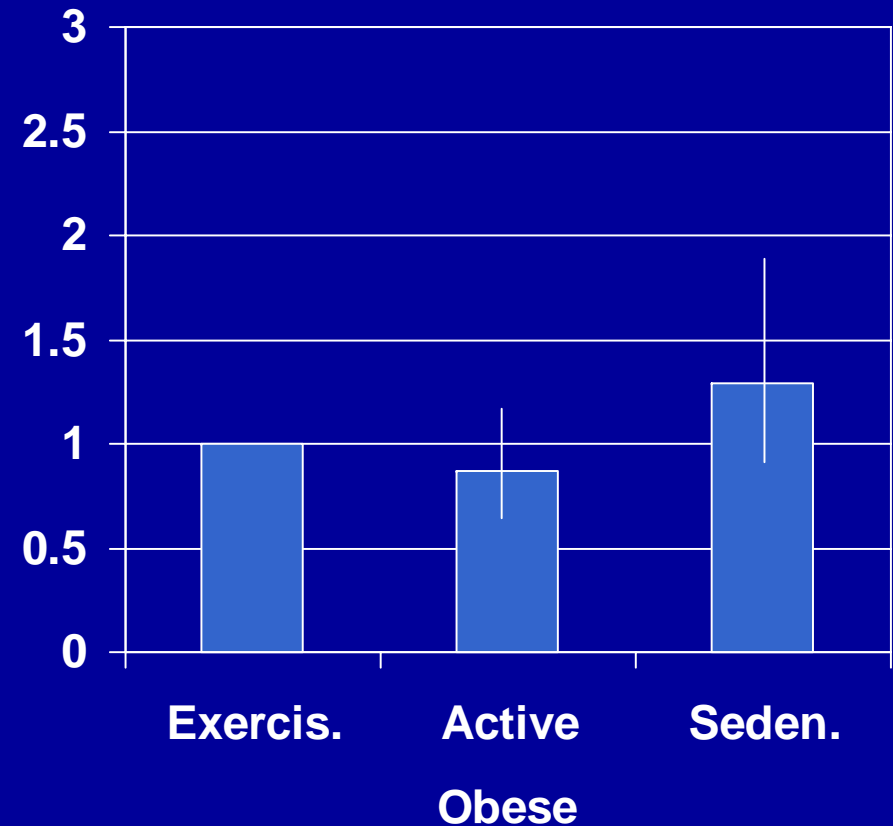
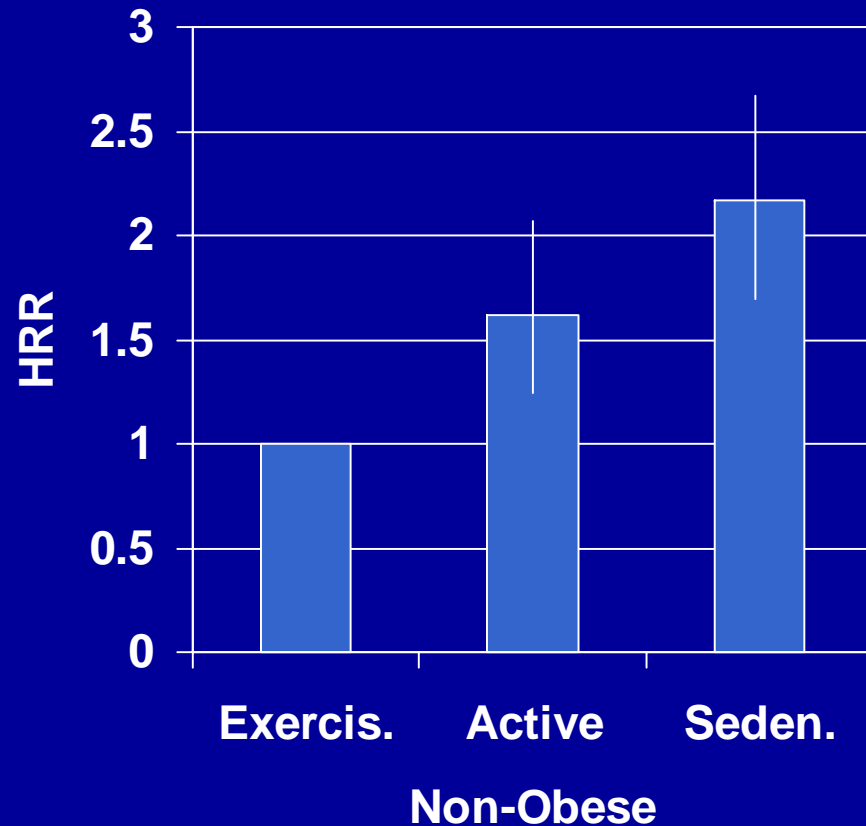
† Regression coefficient (standard error)

Ding J, 2005

# Comparing changes in lean mass between those with and without developing mobility limitations

	Lean mass	
	Regression coefficient (standard error)	p-value
Men		
Age, kg/year	-0.215 (0.035)	<0.0001
Age <sup>2</sup>	-0.005 (0.002)	0.019
Age*mobility limitation	-0.035 (0.028)	0.20
Women		
Age, kg/year	-0.079 (0.026)	0.003
Age <sup>2</sup>	-0.001 (0.002)	0.43
Age*mobility limitation	-0.043 (0.019)	0.02
* Including birth cohort, age, age <sup>2</sup> , race, site, height, mobility limitation, age*mobility limitation, body fat, and lean mass at baseline in mixed model		

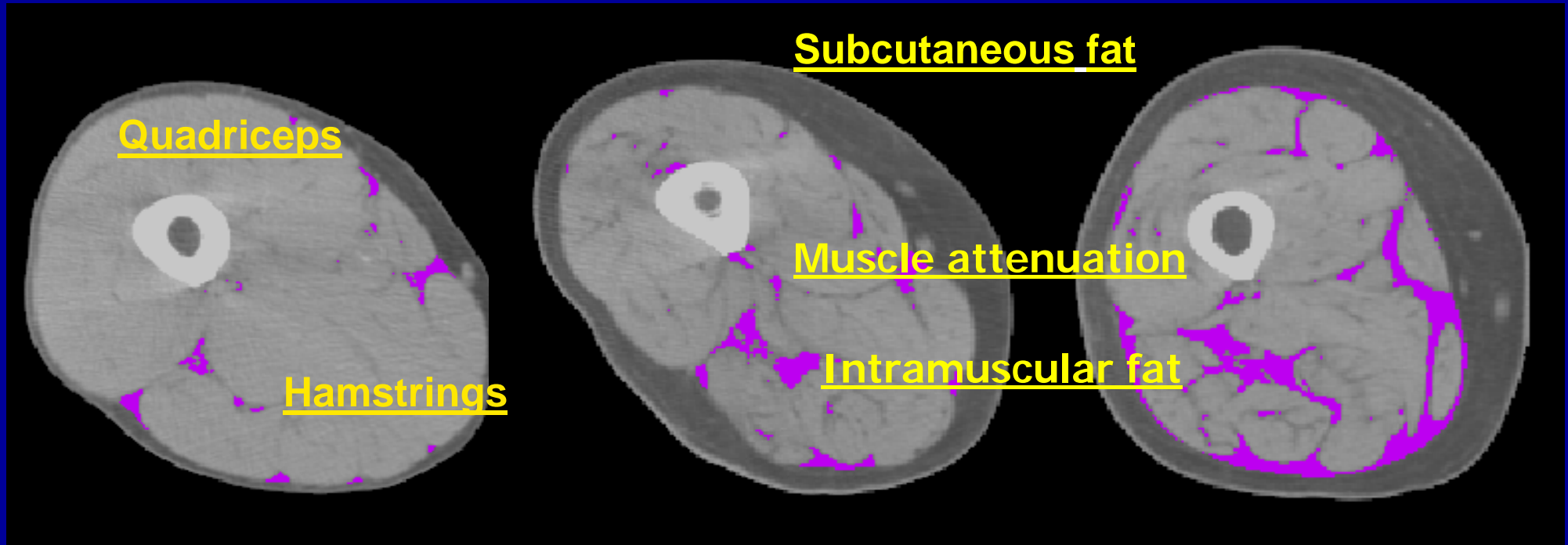
# Adjusted\* hRR for Incident Mobility Limitation by Exercise and Obesity Status



\*Adjusted for demographics and comorbid illnesses.

(Koster, in prep)

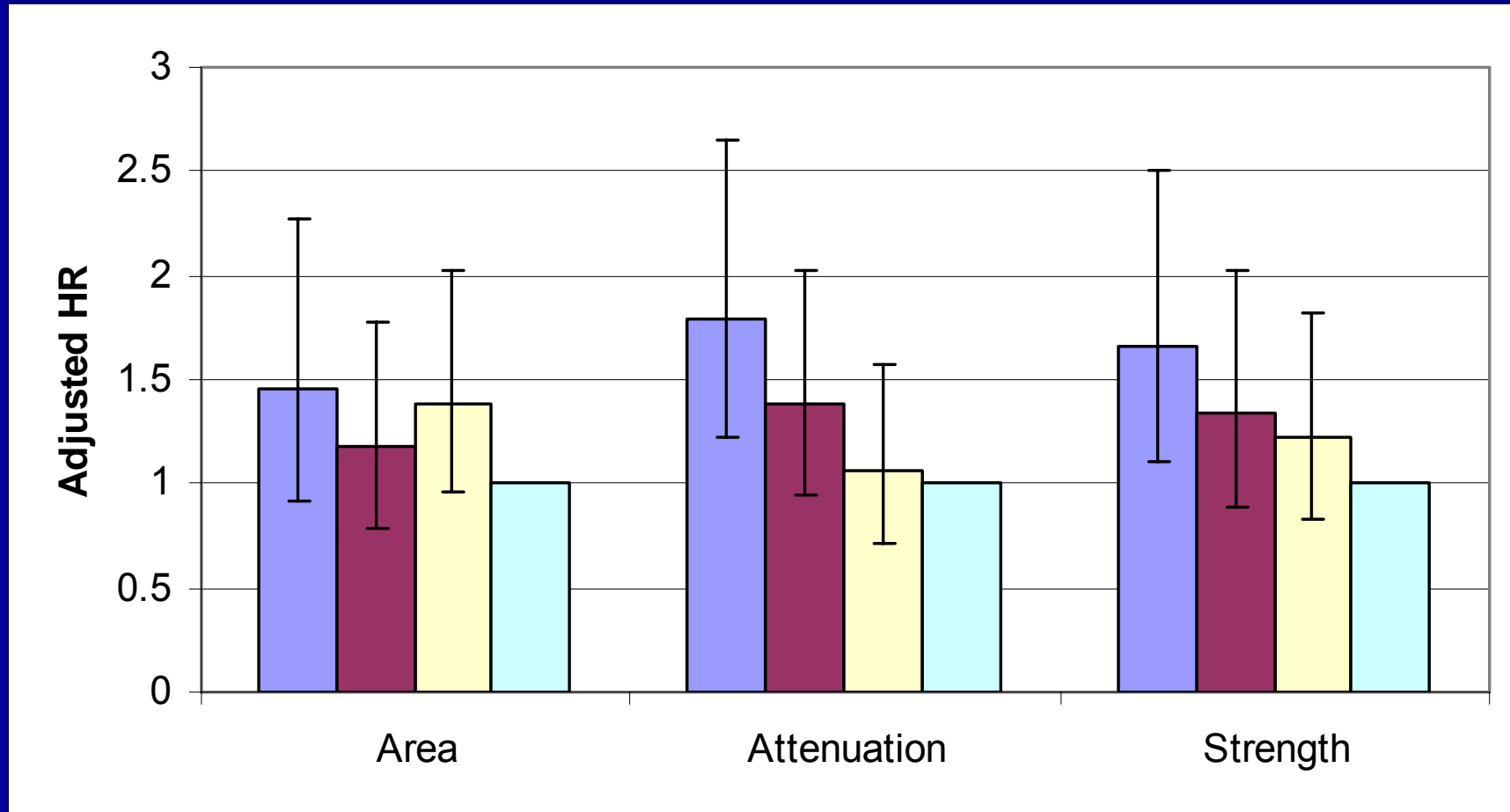
# Computerized tomography of the mid-thigh: Health ABC



Intramuscular fat-Pools of lipid within fascial planes

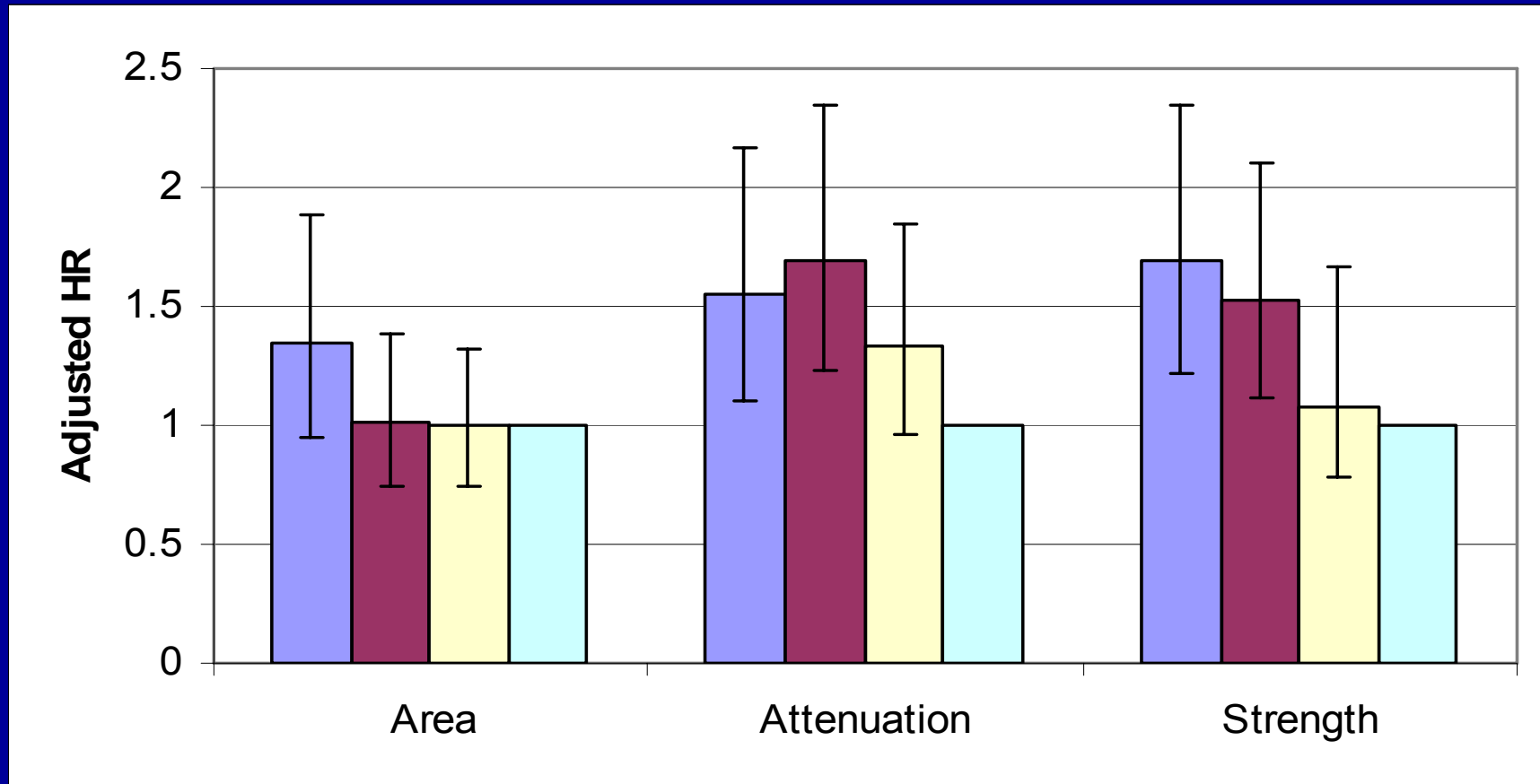
Muscle attenuation- Reflects both intramyocellular lipid and extramyocellular; the greater the lipid, the lower the attenuation.

## Adjusted Hazard Ratios for Incident Mobility Limitations According to Quartiles of Three Muscle Parameters: Health ABC - MEN



Adjusted for: age, race, site, height, total fat mass, education, alcohol, smoking status, physical activity, prevalent disease, self-rated health, depression, cognition and other parameters.

## Adjusted Hazard Ratios for Incident Mobility Limitations According to Quartiles of Three Muscle Parameters: Health ABC - WOMEN



Adjusted for: age, race, site, height, total fat mass, education, alcohol, smoking status, physical activity, prevalent disease, self-rated health, depression, cognition and other parameters.

# Incidence of Limitation by Physical Activity and Genotype

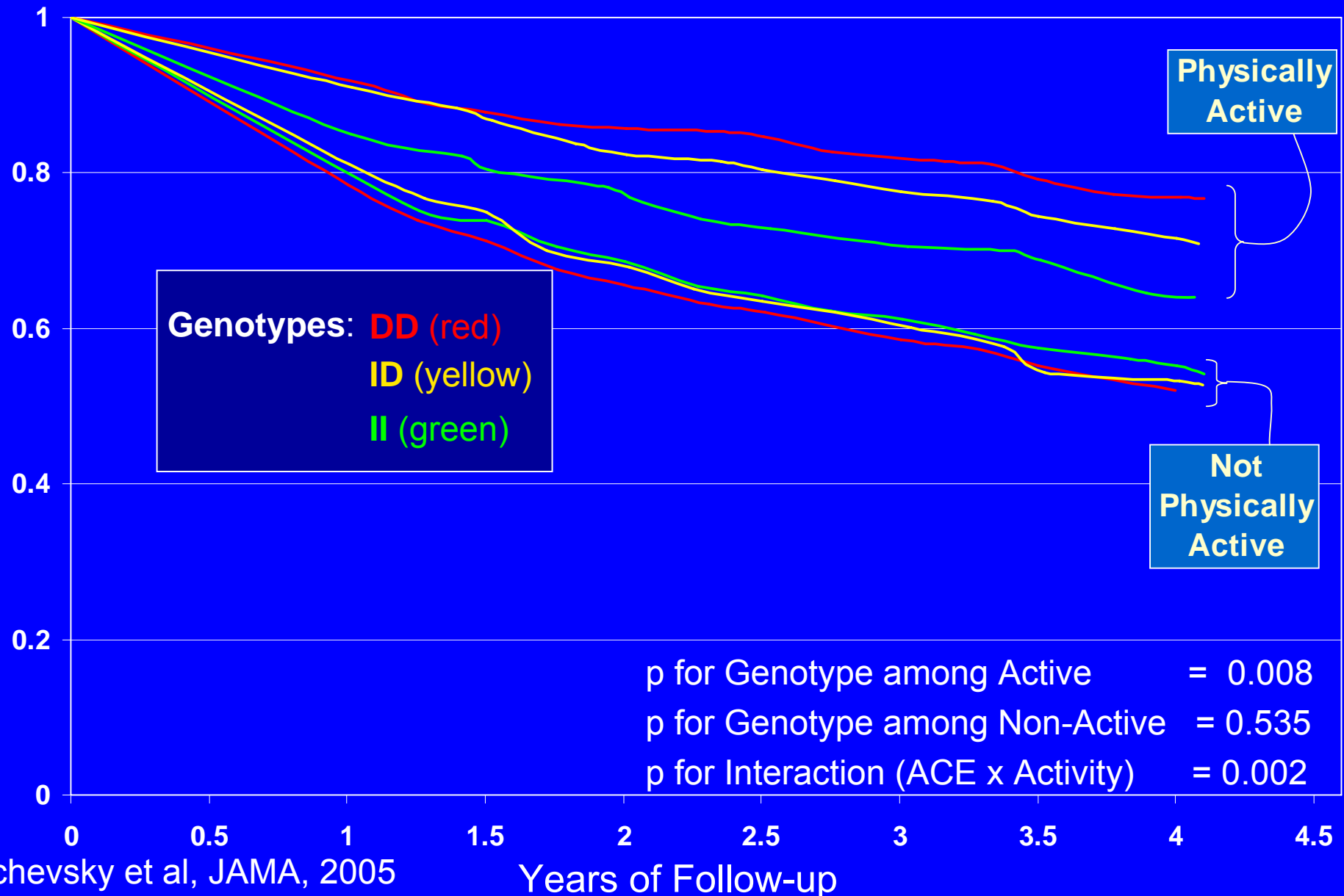
Physically Active	Yes	No
4-year Incidence (%)	27.9	46.3

$p < 0.001$

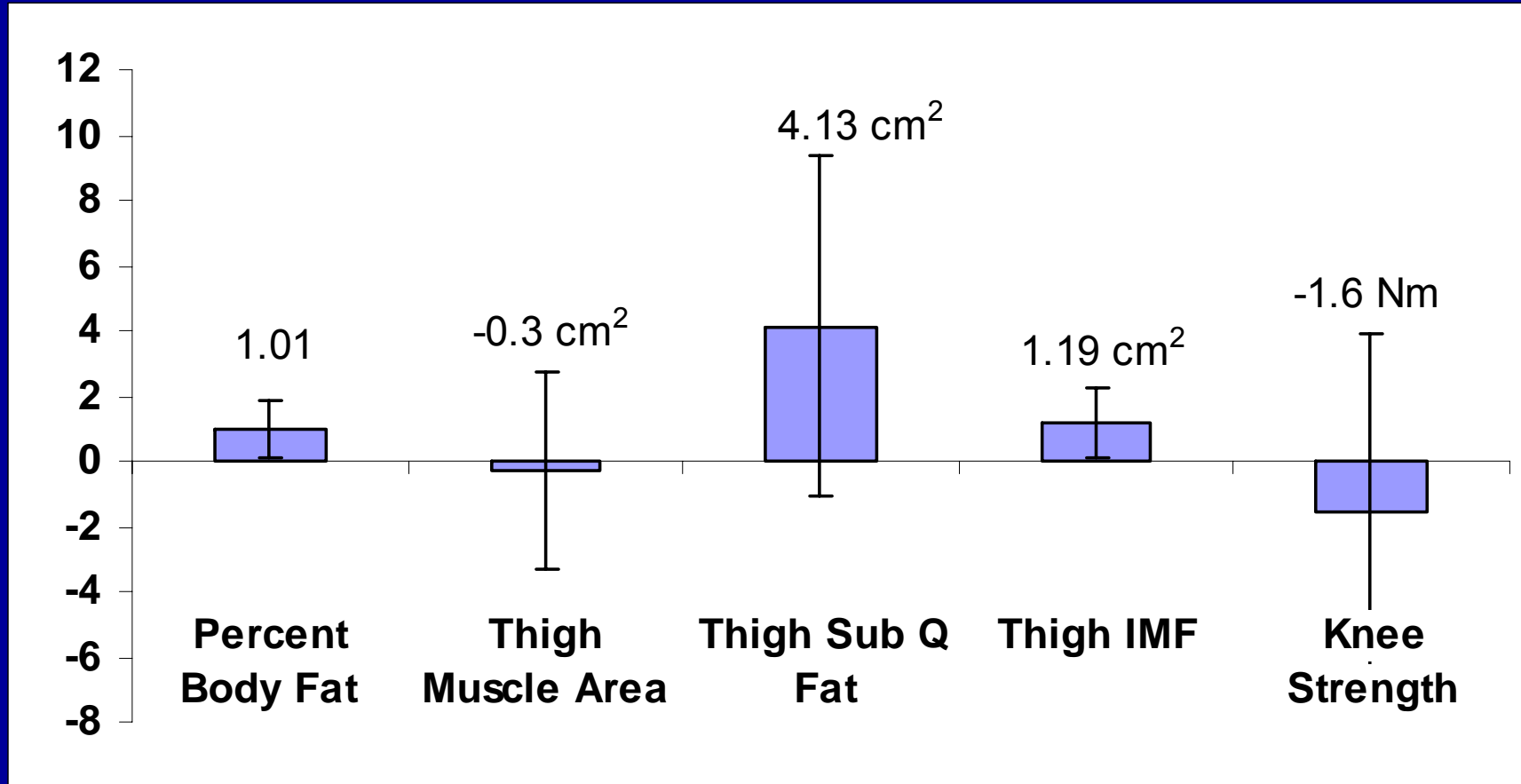
Genotype	DD	ID	II
4-year Incidence (%)	39.9	40.0	43.1

$p = 0.31$

# Survival Curves for Onset of Lower Extremity Limitation by ACE Genotype and Physical Activity

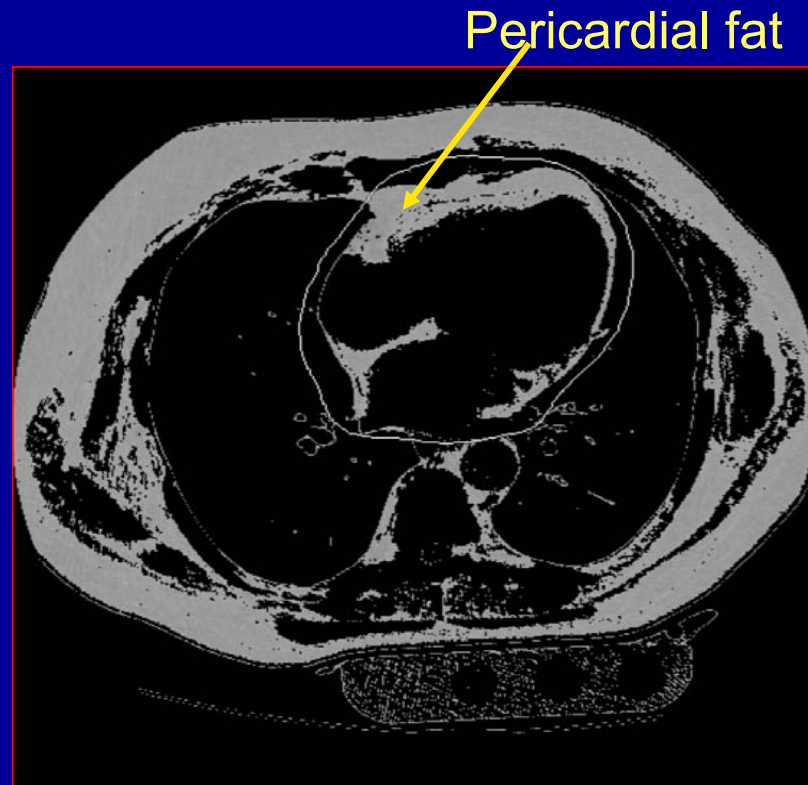


# What Might Explain the Reduced Benefit of Exercise for the II Genotype?



II-ID/DD differences adjusted for age, race, gender, gender-race interaction, and site

# Cardiac CT scan



Association of fat measures (a standard deviation as the unit) with the presence of calcified coronary plaque in 79 women participating in the MESA study.

	Odds ratio (95% CI)
Model 1*	
Pericardial fat, 29.24 cm <sup>3</sup>	1.90 (1.21, 2.97)
Model 2	
BMI, 4.16 kg/m <sup>2</sup>	1.00 (0.70, 1.44)
Model 3*	
Waist circumference, 11.71 cm	1.18 (0.83, 1.70)

\* Adjusting for height

# Sarcopenia (Annotated)

- Muscle mass is lost progressively after young to mid-adulthood. Fat mass generally and central adiposity particularly increases progressively with age.
- Muscle mass correlates with strength.
  - Fatty infiltration of the muscle correlates with strength and predicts functional decline.
- Low strength is a hallmark of disability
  - Low strength in relation to total body weight is also important.
- Many disabling conditions are associated accelerated with the loss of lean mass.
  - Many disabling conditions are associated with ectopic fat. Fat is a major source of cytokines which: a) predict the onset of many disabling conditions, and b) are hypothesized to accelerate muscle catabolism.

# *NHLBI Obesity Education Initiative*

“There is little evidence at present to indicate that obesity treatment should be withheld from adult men and women on the basis of age alone up to 80 years of age.”

“However, the weight control program must often be individually tailored to have a desirable outcome. This would include preservation of body cell mass and its function, and loss of fat mass.”

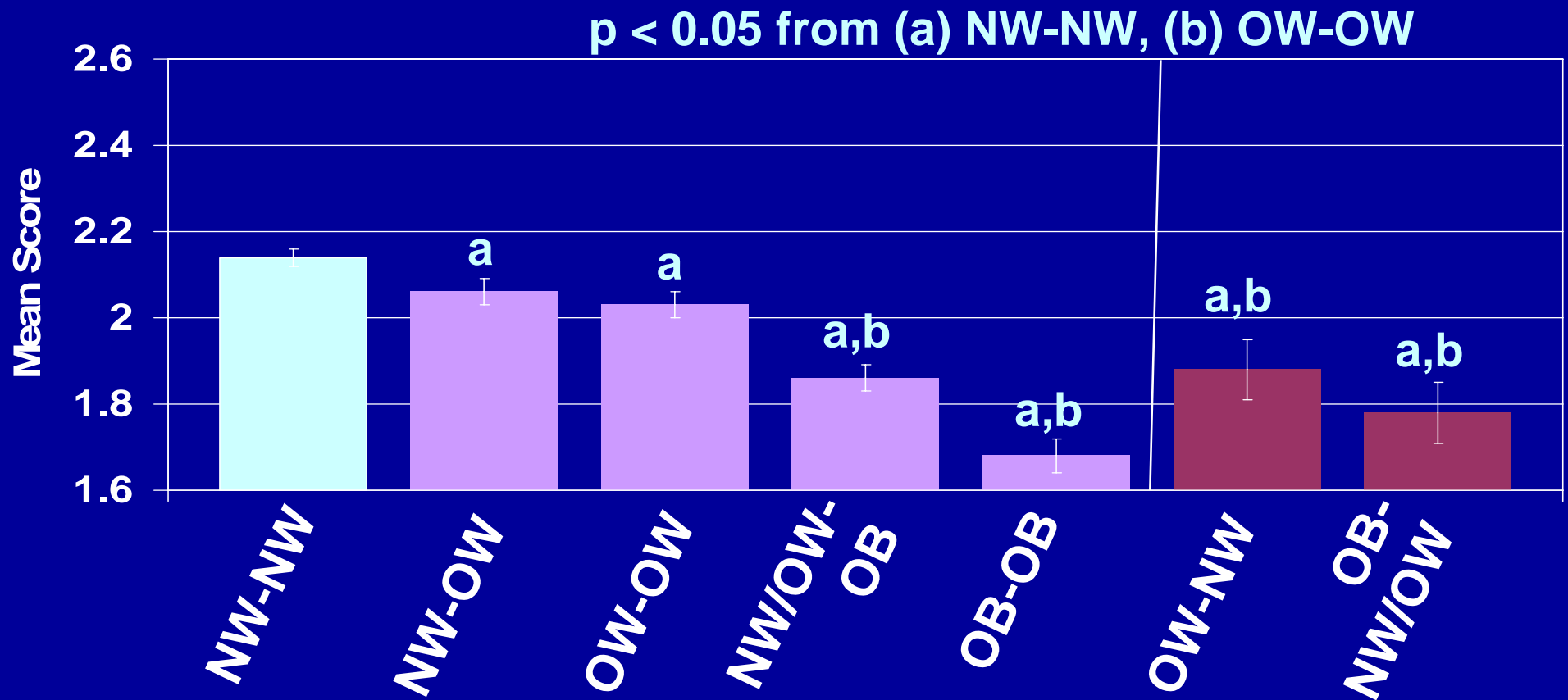
# “Weight loss in older adults is dangerous because . . .”

Weight loss is associated with the onset of severe illness in older adults.

Excess weight represents a reserve that helps older adults to survive serious illnesses.

Weight loss will decrease bone density increasing the risk of fracture.

# Adjusted SPPB Scores by Weight History Patterns in Women



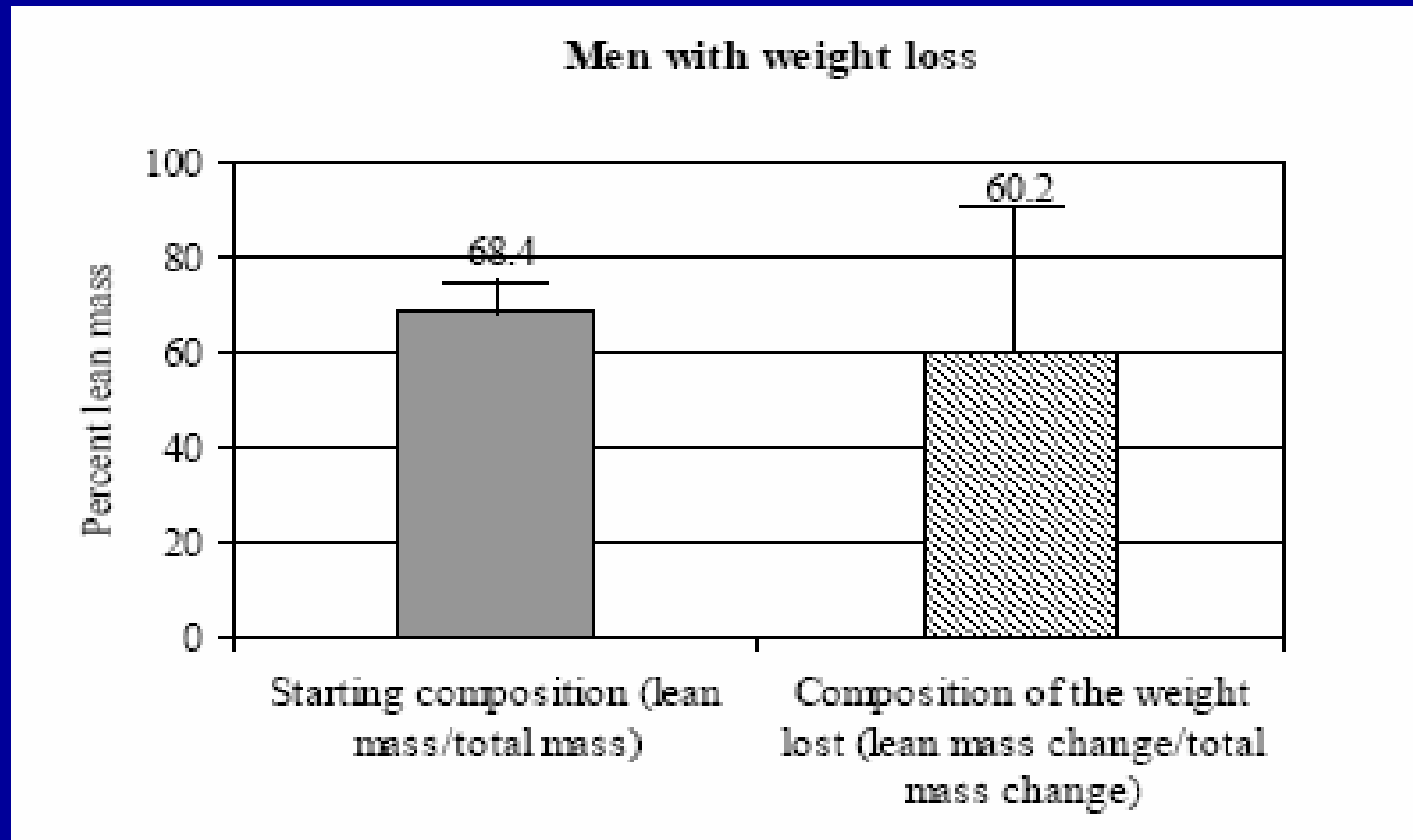
Adjusted for: age, race, site, education, physical activity, and smoking status

Houston, 2005

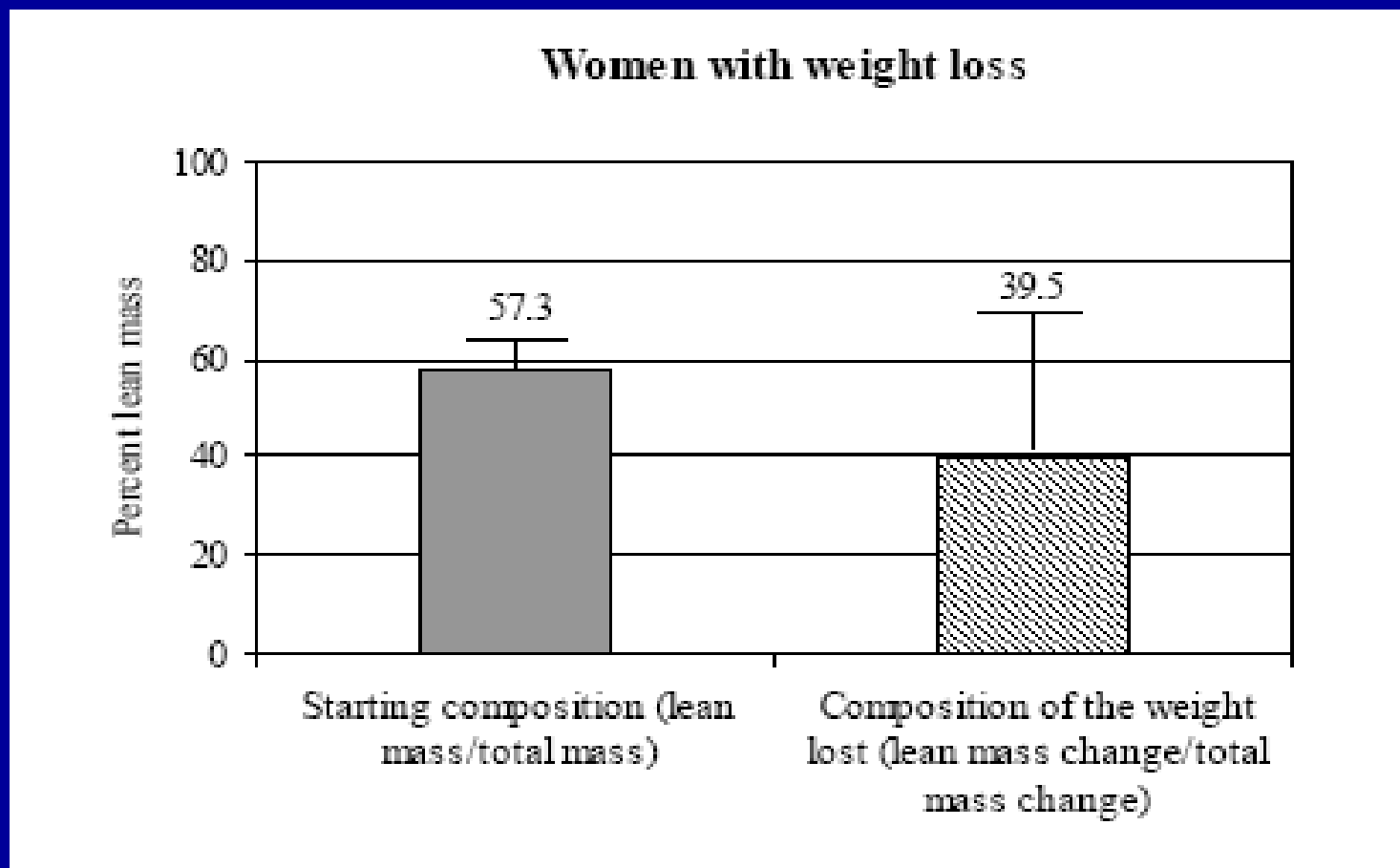
# The Ideal Intervention

- Spares skeletal muscle mass
- Spares bone
- Targets ectopic fat depots

# Composition of Mass Change Among Older Men Losing $\geq 3\%$ Body Weight Over 4 Years – The Health ABC Study



# Composition of Mass Change Among Older Women Losing $\geq 3\%$ Body Weight Over 4 Years – The Health ABC Study



# Weight Loss and LBM Loss in Older Overweight Women – DEMO interim results

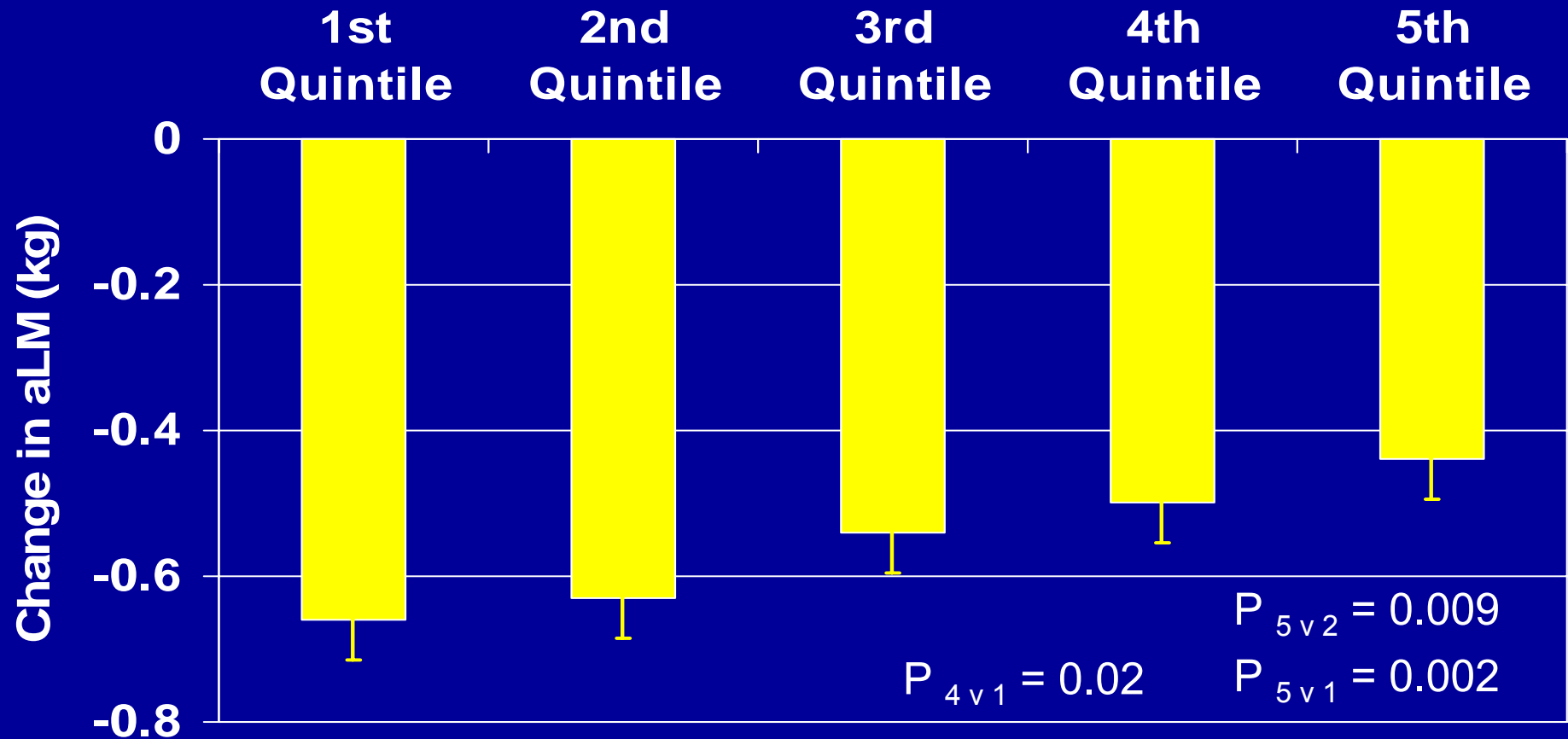
Group	Total Mass Lost	Lean Mass Lost	Weight Lost as Lean Mass
Diet Alone	-11.6 kg	4 kg	35.6 %
Diet and Low Intensity Aerobic Exercise	-11.5 kg	3.6 kg	33.4 %
Diet and High Intensity Aerobic Exercise	-9.9 kg	3 kg	27.1%

B. Nicklas, personal communication

# Sparing Muscle/Bone

- Dietary Protein
- Resistance Exercise
- Growth Hormone, Testosterone
- Anti-Resorptive Therapy

# Adjusted 3-year aLM Loss by Quintiles of Energy-Adjusted Dietary Protein Intake



Adjusted for gender, race, age, site, height, baseline aLM, physical activity, smoking, energy intake, CHD, pulmonary disease, diabetes and oral steroid use.

$P_{\text{overall}} = 0.01$

# Protein Intake and aLM: Subgroups of Interest

Subgroup	% of Sample	Beta (SE)	p-value
Overall		4.3 (1.6)	0.007
Men*	47.5	1.5 (2.4)	0.52
Women	52.5	8.4 (2.2)	<0.001
Low Phys Activity**	49.0	1.2 (2.5)	0.61
High Phys Activity	51.0	6.6 (2.1)	0.002
Weight Losers§	53.4	3.1 (2.0)	0.12
Weight Gainers	46.6	4.2 (1.9)	0.03

Adjusted for gender, race, age, site, height, baseline aLM, physical activity, smoking, energy intake, CHD, pulmonary disease, diabetes and oral steroid use.

\*P<sub>int</sub> = 0.09; \*\*P<sub>int</sub> = 0.10; §P<sub>int</sub> = 0.62

# PROMO

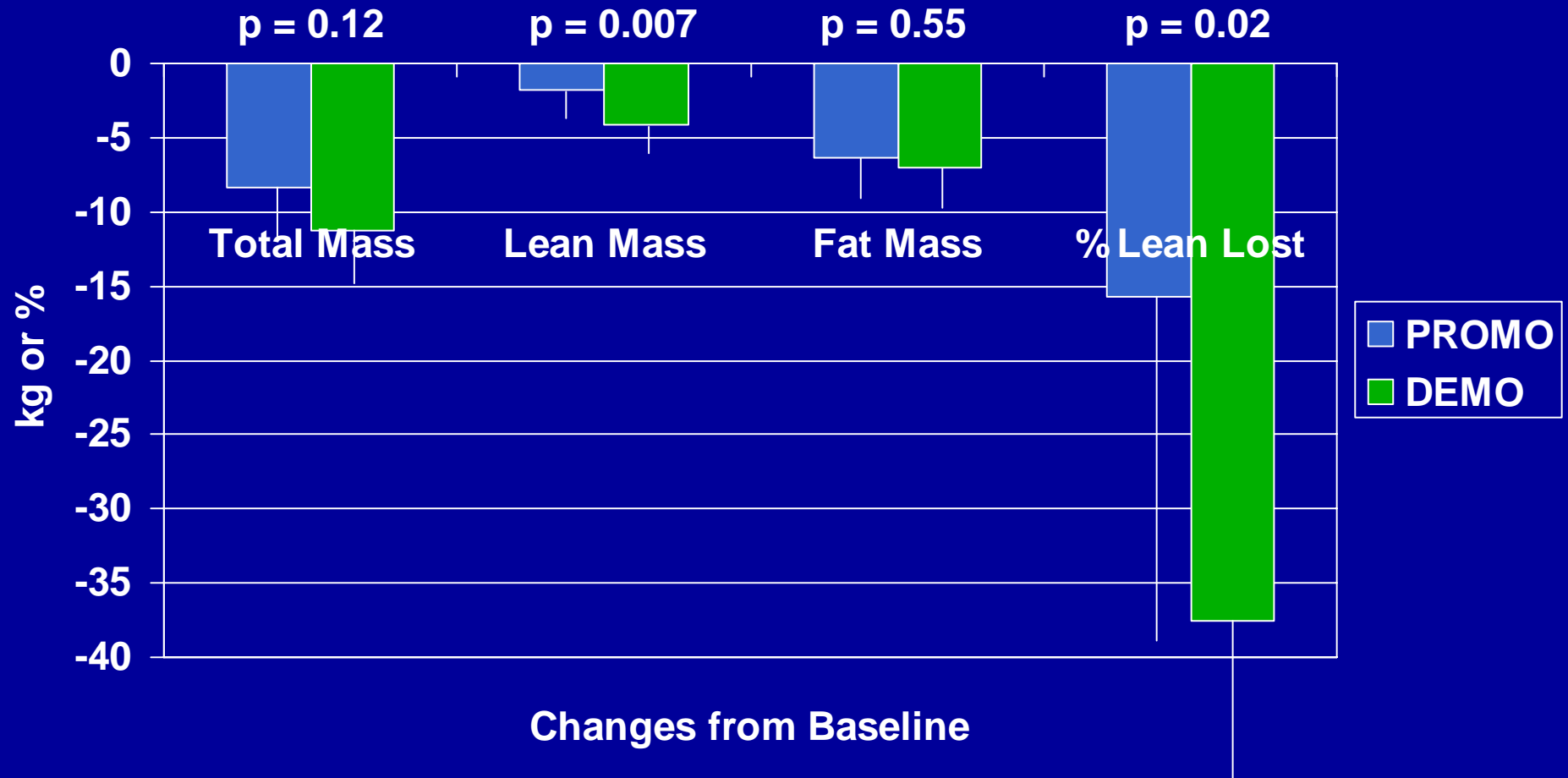
- Mirrors caloric deficit of DEMO (400 kcal/day)
- Protein intake is fixed to initial LBM
  - $\sim 1.2 \text{ g}/(\text{kg} \cdot \text{d})$  vs.  $0.7 \text{ g}/(\text{kg} \cdot \text{d})$
- Lunches and dinners provided by GCRC metabolic kitchen
- 12 women enrolled and 9 completed

# PROMO Baseline Characteristics

## Mean (SD)

	PROMO (n=9)	DEMO (n=15)	p-diff
Age (yrs)	57.1 (6.1)	58.6 (6.8)	ns
% African-American	67%	60%	ns
Total Mass (kg)	85.5 (9.3)	93.5 (8.2)	0.04
% Body Fat	42.2 (3.2)	42.4 (4.1)	ns
% Lean BM	55.3 (3.1)	55.1 (4.1)	ns

# PROMO – Mean Changes (SD) in Body Composition from Baseline



# Effects of weight loss on muscle mass & strength:

## A 6-month randomized, controlled pilot study in older, obese men & women

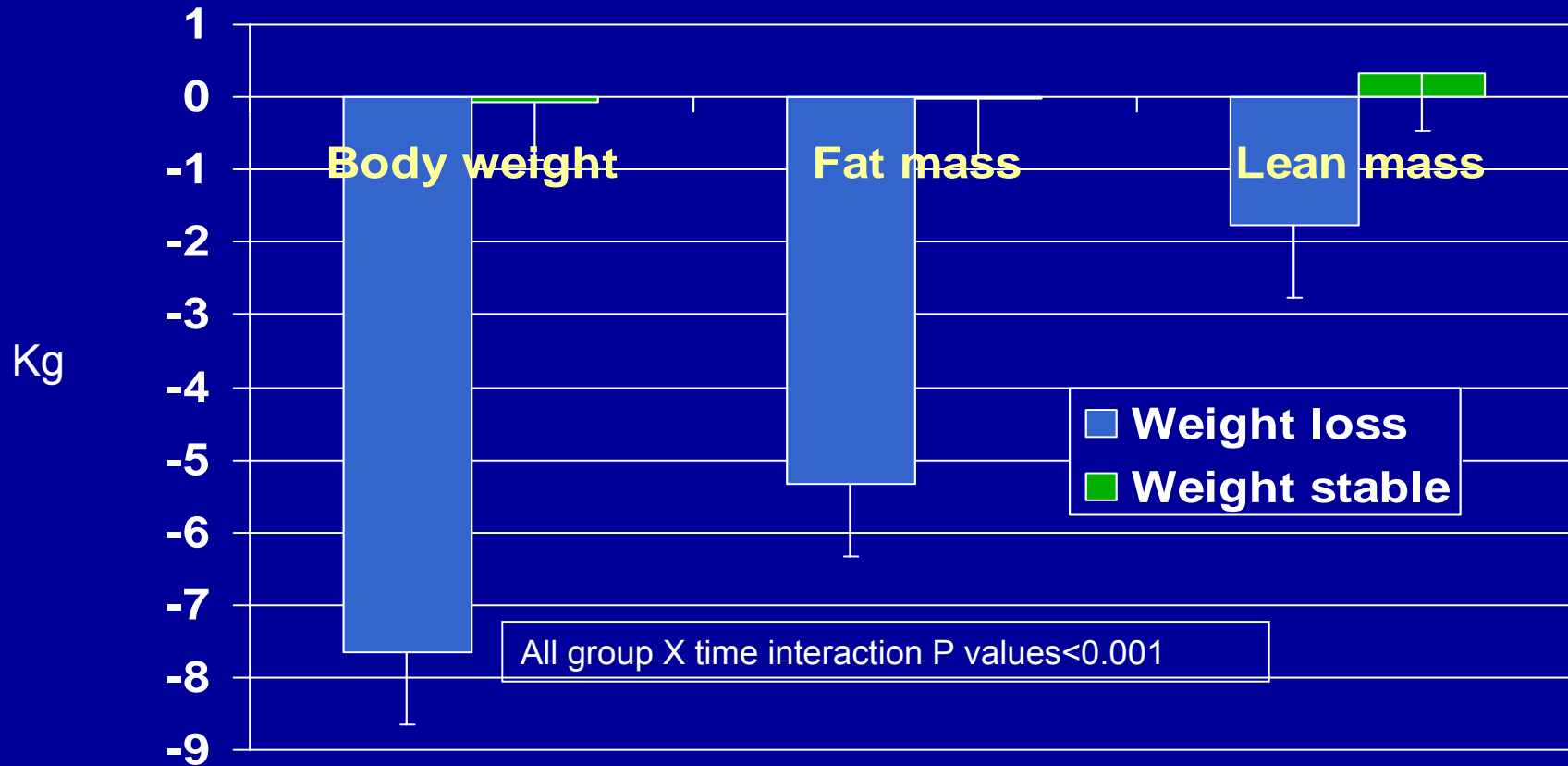
### Participants:

- Age  $\geq 60$  yrs; Mean age =  $69.5 \pm 5.7$  yrs
- BMI  $\geq 30$  kg/m<sup>2</sup>; Mean BMI =  $35.3 \pm 7.3$  kg/m<sup>2</sup>
- knee pain & radiographic evidence of knee OA
- self-reported physical disability
- sedentary ( $< 20$  min/wk) for the past 6 mo
  
- 62% female
- 83% Caucasian
- N=87 randomized; N=68 completed interventions and follow-up

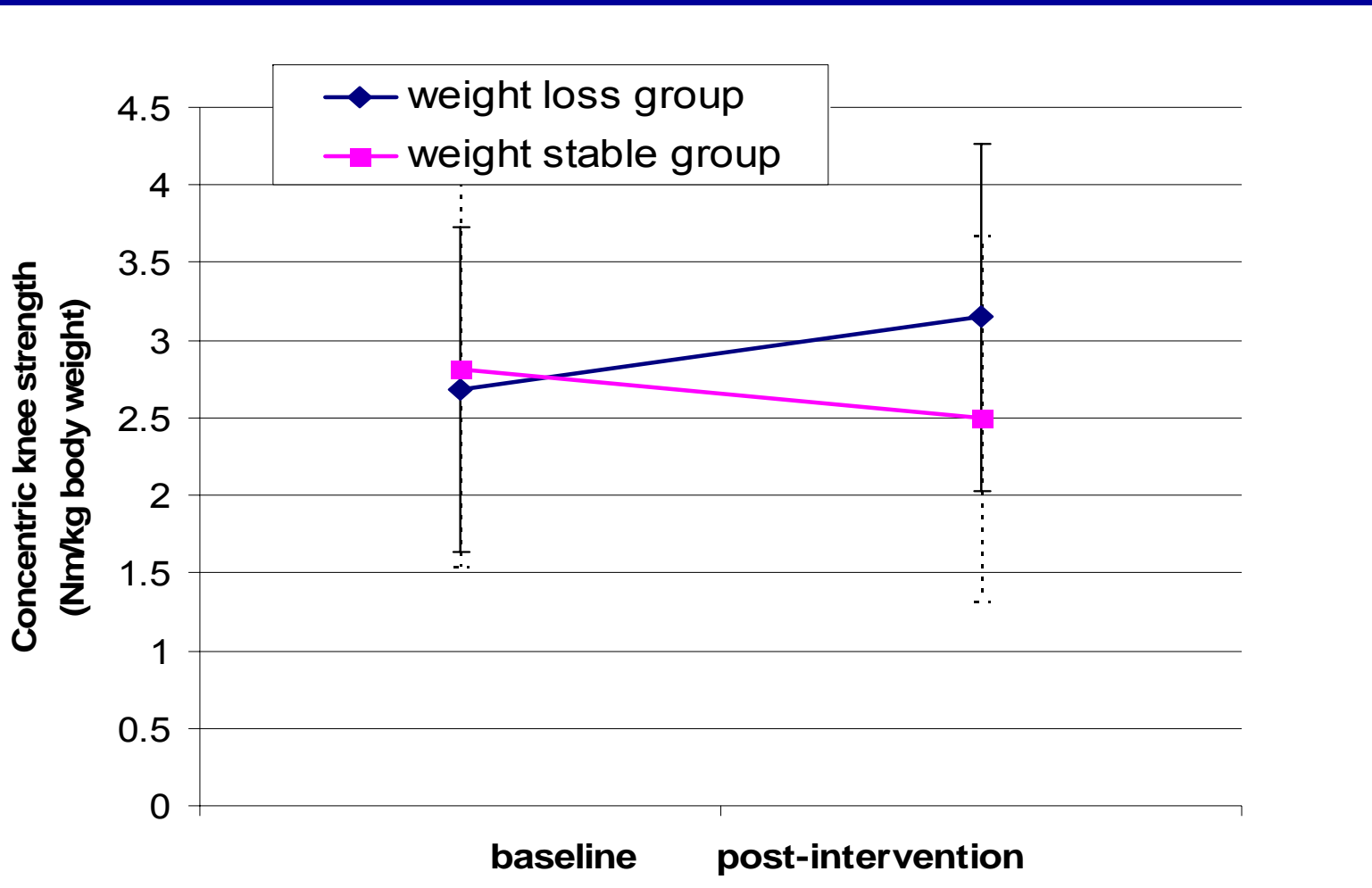
# Weight loss in older men and women

- Weight loss intervention (WL):
  - 10-12% weight loss goal
  - Weekly nutrition education meetings
  - Energy-restricted diet via meal replacements (SlimFast®) for 2 meals/day with a structured meal plan for remaining meal
  - Center-based aerobic and light resistive training (3 days/wk; 60 mins/session)
- Control/Weight stable (WS):
  - Asked to maintain initial body weight
  - Bimonthly group meetings on health topics not related to diet/exercise

# Body composition results



# Concentric knee strength results



# Muscle strength, Muscle Size and Mortality risk in Health ABC Women

	HR (95% CI) unadjusted	HR (95% CI) multivariate adjustment including body composition (for strength)
<b>Muscle</b>		
CT leg muscle area (per 28.1 cm <sup>2</sup> )	1.19 (0.86-1.64)	0.94 (0.66-1.35)
DEXA arm lean (per 0.9 kg)	1.12 (0.74-1.70)	1.00 (0.61-1.65)
<b>Strength</b>		
Quadriceps strength (per 38.0 Nm)	1.65 (1.19-2.30)	1.56 (1.05-2.30)
Grip strength (per 10.7 kg)	1.84 (1.28-2.65)	1.67 (1.08-2.58)

(Newman et al. J Gerontol, 2006)

# Candidates for Targeting Ectopic Fat Depots

Thiazolidinediones (PPAR- $\gamma$  agonists)

- ACE inhibitors / ARB Blockers (?)
- Conjugated Linoleic Acid ( $\pm$ )

# Effect of Pioglitazone Treatment on Abdominal Fat Distribution in Middle-Aged Diabetic Men and Women

Body Composition Parameter (n=13)	Before Pioglitazone	After 16 wks of Pioglitazone (45 mg/d)	P-value
Fat Mass (kg)	27 ± 2	30 ± 3	0.001
Fat Free Mass (kg)	55 ± 3	55 ± 3	1.0
Abdominal Subcutaneous fat area (cm <sup>2</sup> )	301 ± 44	342 ± 44	< 0.001
Visceral fat area (cm <sup>2</sup> )	144 ± 13	131 ± 16	0.04

# Keep in mind . . .

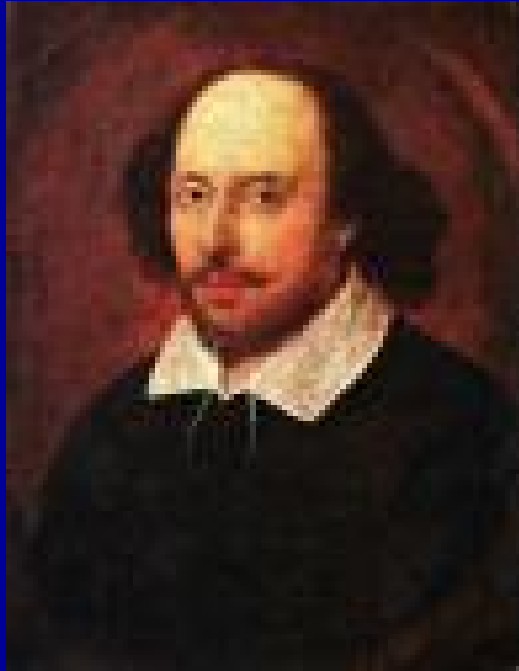
- Health ABC represents the highest functioning ½ of older adults.
- The relative importance of fat and muscle may depend upon where on the functional spectrum you begin.



# In conclusion . . .

- The concept of sarcopenia needs revising in light of recent findings regarding the importance of fat in functional health.
- Such a revision suggests additional interventional avenues for disability prevention in older adults.





“Thou seest I have more flesh  
than another man, and therefore  
more frailty”

Falstaff

*King Henry IV, pt 1 Act III, Scene III*

# Muscle strength, Muscle Size and Mortality risk in Health ABC Men

Strength	HR (95% CI) unadjusted	HR (95% CI) multivariate adjustment including body composition (for strength)
<b>Muscle</b>		
CT leg muscle area (per 28.1 cm <sup>2</sup> )	1.32 (1.09-1.61)	1.26 (1.02-1.55)
DEXA arm lean (per 0.9 kg)	1.06 (0.84-1.33)	1.00 (0.76-1.33)
<b>Strength</b>		
Quadriceps strength (per 38.0 Nm)	1.51 (1.28-1.79)	1.36 (1.12-1.65)
Grip strength (per 10.7 kg)	1.36 (1.13-1.64)	1.36 (1.10-1.60)

(Newman et al., 2006)